AMEBIASIS*

COMMENTS ON VARIOUS AMEBACIDES
REPORT OF CASE

By HAMILTON H. ANDERSON, M. D.
AND
ALFRED C. REED, M. D.
San Francisco

DISCUSSION *by John F. Kessel, Ph. D., Los Angeles; Herbert Gunn, M. D., San Francisco.*

SINCE the recognition of *E. histolytica* as the cause of endemic dysentery, attention has been focused on treatment. A variety of drugs and methods have been advocated which it is unnecessary to review here. More general satisfaction probably has been expressed with ipecac and emetin than with any other single drug type of therapy. Emetin seems to have approached nearest to the requirements of a specific cure but has fallen short in certain important particulars. These are the limited percentage of cures by the use of emetin alone, and the unpleasant symptoms and high toxicity of the drug itself for the patient. The necessity of hypodermic administration is a disadvantage, compared with a drug of similar effectiveness which could be given by mouth to ambulatory patients. A discussion has been made of the symptoms and dangers of emetin poisoning,[1] in which the toxic action on the heart muscle and the easy production of peripheral neuritis have been emphasized. Emetin has been a useful but dangerous and not fully satisfactory drug, whose indiscriminate and excessive use has become an abuse with serious damage to many patients.

The effectiveness of other drugs proposed for the eradication of *E. histolytica*, as judged by percentage of cures, has been relatively low in spite of glowing reports by individual workers. Uniform results of high percentage of cures have in no case been confirmed by sufficient workers in different fields. In many published observations there is little evidence that the curative value of the drug was estimated from a sufficiently long observation of the cases, checked by competent stool examination.

In regard to the criterion of cure, it is to be remembered that amebiasis means invasion of the host by *E. histolytica*, an invasion which has never been proved to occur through any other portal than the colon. The one and only diagnostic sign is the microscopic identification of *E. histolytica*. This organism does not of necessity produce dysentery or even diarrhea, and only in the presence of dysentery or diarrhea ordinarily do the trophozoite or active forms appear. In any case, diagnosis rests preferably on fixed stained preparations showing *E. histolytica*. We have arbitrarily assumed that the organism must be absent from the stools on adequate examination by a competent examiner for a period of at least three months following termination of treatment in order to justify the conclusion of cure having been effected. Remembering the inconstancy of appearance of the cysts, it is evident that numerous examinations must be made over a three months' period at least. Possibility of reinfection must be considered in connection with the personal hygiene and direct exposure of the patient. Review of published cases and groups of cases shows at once how rarely these minimal requirements for a judgment of cure have been met.

So far, then, no satisfactory treatment of amebiasis has been developed. Even various combinations of drugs as, for example, emetin with chiniofon and acetarsone, are not invariably curative and have a definite risk of toxicity. A fully satisfactory treatment should interfere little, if at all, with the usual activity of the patient, should be of such low toxicity as to carry no practical danger of drug symptoms or damage, should be capable of administration by mouth, and should be of low cost. These conditions are not met by any accepted present-day treatment of amebiasis.

For the reasons enumerated, the search for a better drug has been carried on by many workers in recent years and there is hope that the end of the therapeutic trail may be in sight. The case reported here illustrates a common manner of response of amebiasis to various drugs which have been highly advocated for its cure and which really up to this time represent the best available agencies for fighting this infection. The value of the report lies in the length of time during which the patient has been followed, the variety of therapy employed, and the interesting implications to be derived from the frequent stool examinations as related to the treatment and the physical condition of the patient.

REPORT OF CASE

G. S., male, aet, thirty-four, white, married, seaman and laborer.

Complaint.—Dysentery; five to sixteen watery stools daily, with blood, mucus, and abdominal pain, since 1920.

Present Illness.—Six months after trip to Argentina and West Indies patient began having fifteen to sixteen thin, watery, yellow stools daily, containing blood and mucus, and suffered from abdominal pain, not associated with jaundice, tenesmus, nausea, or vomiting. Complained of anorexia, however, and lost thirty pounds weight during the first three years of illness. He was given intramuscular injections in France during this time, with some temporary relief. The presenting symptoms recurred, however, and continued to 1923, when he received anti-amebic therapy, again only temporarily relieving him. In 1925 he was hospitalized again and was given more treatment without lasting benefit. Five years ago the appendix was removed but his symptoms continued, nevertheless. Since then the dysentery has been accompanied by tenesmus, anorexia, loss of weight, fatigability, and weakness of the legs. He was referred to our clinic in February 1930, and his course since that time is shown in the accompanying table. Six months previous to admission the patient had been given a series of intravenous injections and some oral therapy, the exact nature of which is not known.

Family and Marital History.—Negative.

Past History.—He was born in Malta, where he lived for eleven years, then to New York for eight years, and has lived in California since the age of nineteen

* From the Pacific Institute of Tropical Medicine within the Hooper Foundation for Medical Research, University of California, San Francisco.
* Read before the joint meeting of the General Medicine and Pathology and Bacteriology Sections of the California Medical Association at the sixtieth annual session at San Francisco, April 27-30, 1931.
* With the technical assistance of Miss Dorothy A. Koch.

except for a four-year period at sea. The patient denies previous illnesses, but admits having had blood in his stools and "liver trouble" eighteen years ago. Venereal symptoms denied.

Habits.—Moderate smoker, has no food intolerances, and sleeps eight hours nightly.

Weight.—Average 150 pounds, present 146 pounds.

Physical Examination.—Temperature, pulse, and respiration are normal. Height, 5 feet 4 inches, weight 143 pounds. The patient is a poorly nourished adult, white male, apparently chronically ill. The skin and mucous membranes are pale, anterior cervical lymph nodes are palpable. Several carious teeth are present, with marked retraction of the gums. Chest is essentially negative, heart is not enlarged, pulse is regular, and blood pressure 120/70. The abdomen is full, soft, and well muscled, with a healed scar in the R. L. Q. and definite tenderness in the L. L. Q. along the descending colon and cecum which is palpable. Liver and spleen are not felt. Extremities are negative except for exaggerated patellar reflexes.

Laboratory Findings.—Blood Wassermann, reaction negative. Urine, negative. Blood: hemoglobin, 75 per cent (Sahli); red cells, 4,350,000; white cells, 9650 with 70 per cent neutrophils, 19 per cent lymphocytes, 6 per cent monocytes, and 5 per cent eosinophils. Stool: watery, brown, with blood and mucus, positive for motile *Entamoeba histolytica.* Phenosulphophthalein kidney function test:

	Cubic Centimeters	Per Cent
First hour	125	35
Second hour	100	15
Total	225	50

Icterus index, 14. Electrocardiogram, rate 52, S. A. bradycardia with sinus arrhythmia, within normal limits. X-ray, gastro-enteric studies reveal no organic lesion, except spasticity of the colon. Films of gallbladder are negative.

COMMENT

In Table 1 the progress of the patient is reported during the course of the present illness. It is to be noted that almost every promising drug proposed for use in amebiasis during the past twenty years has been tried without avail, with one exception. "Carbarsone," which is carbaminophenylarsonic acid,[2] has improved the patient subjectively and has cleared the stools of *Entamoeba histolytica* for more than eleven months following the last dose of the drug. The patient has gained weight, is free of symptoms, and has shown no evidence of toxicity from arsenic.

No practical conclusions should be drawn from the results of therapy in one case of amebiasis, but it may be said, however, that we have had comparable effects from "carbarsone" in a series of forty patients who have had a proper period of observation for three months after treatment. We expect to report such a group of patients soon, but present this case in detail to indicate the variety of response in an individual patient to the various amebacides which are recommended.

SUMMARY

1. The therapy of amebiasis has heretofore been unsatisfactory.

2. The most effective drugs in general use, especially emetin, are not certainly curative and easily cause serious toxic symptoms.

3. A case is reported in which a great variety of drugs had been employed repeatedly without success, and in which a "cure" apparently followed the intensive use of a hitherto unused synthetic arsenical, "carbarsone" (carbaminophenyl arsonic acid).*

University of California Medical School.
350 Post Street.

REFERENCES

1. Reed, A. C.: Am. J. M. Sc., 181:553, 1931. Rhinehart, J. F., and Anderson, H. H.: Arch. Path., 11:546, 1931. Anderson, H. H., and Leake, C. D.: Am. J. Trop. Med., 10:249, 1930.

2. Supplied through the courtesy of the Lilly Research Laboratories, Indianapolis. For previous reports on this drug, see: Leake, C. D., Koch, D. A., and Anderson, H. H., Proc. Soc. Exper. Biol. and Med., 27:217, 1930; Chen, M. Y., Anderson, H. H., and Leake, C. D., ibid., 28:145, 1930.

DISCUSSION

JOHN F. KESSEL, PH. D. (University of Southern California, Los Angeles).—This special study of the treatment of a single case of amebiasis may illustrate one of two types of cases which are commonly encountered. First, the case which has received inadequate treatment for amebiasis and has passed from the hands of one inexperienced physician to another, or second, the case which has actually proved resistant to adequate treatment with an accepted amebacide. It would appear from the history that the latter picture obtains in this instance. In looking over the list of early treatments employed in this case it is of interest to note that emetin in some form or other was the drug most commonly used and it would appear that dosage generally recognized to be sufficient was employed at least on two different occasions. The fact that the case did not respond to emetin illustrates the experience common to many, that for chronic intestinal amebiasis emetin in doses which can be tolerated by most patients is often ineffective. This fact, however, does not rule out the use of emetin in amebic dysentery and in amebic hepatitis, where it produces dramatic results. Arsenicals other than stovarsol were used in the early treatment and chiniofon or yatren was employed, but when given orally insufficient amounts to produce a cure were administered. Personal experience in following up one hundred cases treated with yatren in the Peking Union Medical College in which 90 per cent responded to the treatment led to the conclusion that this drug is a very satisfactory treatment for chronic amebiasis. It was not, however, as effective against other of the intestinal protozoa as against *Entamoeba histolytica.* As a consequence cases of mixed protozoal infection and cases resistant to yatren were treated with a combination of yatren and stovarsol. Three grams of yatren were given by mouth on the odd days and .37 grams of stovarsol were given on the even days for a period of two weeks. This treatment proved especially effective and recently in the Los Angeles General Hospital in a series of twenty-five cases so treated and followd up by Dr. C. L. Davison and myself a remarkably high incidence, both of protozoölogical and of clinical cures, has resulted.

The attempt here reported on the part of Doctors Anderson and Reed to employ an effective treatment for amebiasis which will produce the minimum toxicity to the patient and the maximum amebacidal results is to be commended for this is a marked need in the field of therapy in protozoiasis. It is to be hoped that their report of additional cases will show the same effective results reported in this instance.

HERBERT GUNN, M. D. (2000 Van Ness Avenue, San Francisco).—The effort of the authors to find a drug which will be amebacidal and at the same time non-

* Since this case was presented before the California Medical Association on April 30, 1931, the patient has been examined at frequent intervals. Clinically he is cured, and ten stool examinations from May 1 to November 12, 1931, have been negative for Entamoeba histolytica. During the past eleven months, then, following the last dose of carbarsone, the patient has been clinically well for the first time since the onset of his infection in 1920.

TABLE 1.—*Response of Patient to Various Amebacidal Agents*

Date	Stool Examinations*	Treatment	General Condition and Response to Therapy
1920-1923		Intramuscular injections in France (drug not known)	Fifteen to sixteen watery stools, with blood, mucus, and abdominal pain. Temporary relief.
8-9-23	+E. histolytica (motile)	Emetin HCl (intramuscular) 0.65 gram in eighteen days "Alcresta ipecac" pills (oral) six daily for eighteen days Quinin sulphate 1:1000 solution per rectum, twice daily for eighteen days Bismuth subnitrate (oral) twelve grams daily for eighteen days Neoarsphenamin 0.6 and 0.9 gram (intravenous)	In hospital, 8-9-23 to 9-22-23. Weight on entry 136.5 pounds, on discharge 144.5 pounds. Frequency of stools reduced from five to six daily to one formed movement a day. Relief for two weeks.
10-24-23	+E. histolytica (motile)	Emetin bismuth iodid (oral) 0.2 gram daily for fourteen days	In hospital from 10-24-23 to 10-26-23. Six to seven movements daily with blood and mucus.
2-26-25	+E. histolytica (motile)	Emetin HCl (intramuscular) 0.65 gram in ten days Neoarsphenamin 0.6 and 0.9 gram (intravenous) Emetin bismuth iodid (oral) 0.2 gram daily for ten days	Dysentery persists. In hospital from 2-26-25 to 3-17-25. Weight on entry 144.5 pounds, on discharge 149.0 pounds. Temporary relief.
7-30-29		—	Eight to ten watery stools, with blood, mucus, and abdominal pain.
9-15-29		Intravenous and oral therapy, nature of drugs not known	Symptoms persist.
2-17-30	+E. histolytica (motile)	Treated locally for internal hemorrhoids, referred to us by Dr. Dudley Smith (surgical clinic) following proctoscopy, for investigation	("Ulcerations of rectum which look like amebiasis.")
2-18-30 and 19-30	+E. histolytica (motile)		Weight 143 pounds.
2-20-30	+E. histolytica (motile)	"Kurchi alkaloids" (oral) five grams in ten days.	No symptomatic relief.
2-25-30	Negative		Positive stool on 3-3-30.
3-4-30	+E. histolytica (motile)	"Auremetin (oral) two grams in fifteen days	Blood pressure 120/70, pulse 70. Temporary relief.
3-11-30	Negative		
3-15-30	+E. histolytica (motile)		Two to three formed movements a day without pain, blood or mucus.
3-18-30	+Giardia intestinalis	Emetin HCl (subcutaneous) 0.65 grams in twelve days	Presenting symptoms recurred.
3-29-30	Negative		
4-5-30	+E. histolytica (motile)		
4-8-30	Negative		
4-10-30 to 4-28-30	Negative Negative	Acetarsone (oral) 2.75 grams in eleven days Chiniofon (oral) 7.5 grams in fifteen days	Symptomatic relief. Two formed movements daily, no pain, blood, or mucus. Condition good.
4-12-30	+E. histolytica (culture)		
5-15-30	Negative		Blood pressure 112/72, pulse 70. Presenting symptoms recurred.
6-2-30	(Charcot-Leyden crystals)	Chiniofon (oral) 7.5 grams in ten days Chiniofon (rectal) 50.0 grams in ten days	In hospital from 6-2-30 to 6-14-30. Much improved. One to two formed movements daily, no pain, blood, or mucus.
6-16 to 24-30	Negative	Emetin HCl (subcutaneous) 0.55 gram in fifteen days	Symptoms recurred, i. e., four watery movements daily with blood and mucus, no pain. Blood pressure 138/64, pulse 76.
7-1-30	+Strongyloides stercoralis		In hospital from 7-1-30 to 7-8-30.
7-2 to 10-30	+E. histolytica (motile)	Acetarsone (oral) 5.0 grams in ten days	Excessive perspiration, dermatitis, and pains in joints.

* Fresh stool and fixed wet iron hemotoxylin preparations routinely examined.

TABLE 1.—*Response of Patient to Various Amebacidal Agents (Continued)*

Date	Stool Examinations*	Treatment	General Condition and Response to Therapy
8-5-30	(Culture negative for colon-typhoid group)		Blood pressure 110/68. Weight 152.5 pounds. Three formed movements daily. Symptomatic improvement.
8-28-30	+E. histolytica (motile)		
8-30-30	Negative		Symptoms, four to five watery stools with pain in rectum.
8-31-30 to 9-19-30	Negative Negative	"Carbarsone" (oral) 1.5 gram in five days "Carbarsone" (oral) 1.5 gram in seven days	Two to three watery stools daily, no blood, no mucus.
10-16-30			Six watery stools daily, no pain, no blood, no mucus.
10-24-30	+E. histolytica (culture)		Three watery movements daily with blood and mucus, but subjectively improved. Blood pressure 112/70. Weight 152 pounds.
10-28-30	+E. histolytica (culture)	"Carbarsone" (oral) 3.0 grams in ten days	Five watery stools daily with pain, otherwise no change in condition.
11-1 to 13-30	Negative		"Feels fine," no evidence of arsenic toxicity.
11-22-30	+E. histolytica (cyst and motile)		
11-25-30	Negative	"Carbarsone"† (oral) 6.0 grams in twelve days	Condition improved.
12-7-30 to 3-14-31	Negative (Weekly examinations)		Condition improved. Has three to four formed movements daily, no pain, no blood, no mucus. Blood pressure 132/84, pulse 64. Symptom-free. Gained sixteen pounds in weight. Subjectively improved.
3-20-31	+Strongyloides stercoralis		Weight 159 pounds.
3-28-31	Negative		
4-18-31	Negative		Continues well.
4-28 to 11-12-31	Negative		

* Fresh stool and fixed wet iron hemotoxylin preparations routinely examined.
† Total "Carbarsone" (carbaminophenylarsonic acid) administered from 8-31-30 to 12-7-30 is 12.0 grams, or about 185 milligrams per kilo body weight without exhibition of toxic symptoms.

toxic is certainly commendable. Their remarks regarding the toxicity of emetin are certainly correct. However, it must be remembered that severe toxic effects of this drug are evidenced only when it is given in overdoses or injudiciously. The maximum dose should not exceed .65 grams given over a period of from two to three weeks and it should never under any circumstances be given to ambulant cases. Emetin is one of the most valuable drugs we have in the treatment of amebiasis, but it has distinct limitations. It is of the greatest value in controlling ulcerative lesions produced by the amebae, but it has practically no amebacidal properties if used alone. Amebae recur almost invariably after a treatment with this drug alone although the symptoms may remain absent for a long period of time. Combined with some of the arsenicals, which are amebacidal, increased effectiveness is obtained.

Their statement regarding the ineffectiveness of other drugs, I believe is quite true as regards a great many of the treatments advocated, but this fact in no way justifies the conclusion that no drugs or treatments have been advocated that are efficacious. I would say rather that the treatment of amebiasis if properly carried out has reached a stage of specificity closely approaching that of malaria.

In 1918 I published an article in the CAL. STATE JOUR. OF MED., Vol. 16, p. 240, on the treatment of twenty cases of amebiasis with a combination of emetin hydrochlorid and neoarsphenamin. The cases in this series were checked very carefully over a period ranging from several months to several years. I made the statement at that time that this combination was distinctly amebacidal and that about 80 per cent of cures would result from its use. Since that time I have treated several hundred cases with this combination and I will change my statement of results to 90 per cent of cures instead of 80 per cent.

The treatment as originally published has been modified somewhat in that the dosage of emetin hydrochlorid has been considerably reduced and the neoarsphenamin increased. Other preparations of arsenic are undoubtedly amebacidal to a high degree, for instance acetarsone. I have discontinued the use of this drug on account of the frequency with which toxic symptoms occurred.

A comparatively new drug which is also amebacidal is chiniofon, sold under the trade names of yatren and anayodin. I have used the preparation called anayodin quite extensively in the last few years and have not observed any toxic effects from it. When combined with neoarsphenamin, which may be administered rectally, the results in ambulatory cases have shown more than 90 per cent of cures. Anayodin may also be used in the treatment of dysenteric patients after the symptoms have been controlled with emetin, thus greatly reducing the amount of emetin necessary. The anayodin treatment to be effective must be given in sufficient dosage over a long enough period of time. In the treatment of ambulatory cases about two hundred pills of four grains each, representing a total of about fifty-three

grams of anayodin, is my average dose, given during a period of from four to six weeks. In addition, two or three doses of neoarsphenamin are given, usually by rectum, during the course of treatment. The appearance of diarrhea may necessitate the reduction of the dose of anayodin or its omission temporarily. It may be observed that this dosage of anayodin is about seven times larger than that used by mouth in the authors' case.

Rest, one of our best adjuncts in the treatment of intestinal disturbances, is almost completely lost sight of in most discussions of the treatment of amebiasis. Rest during treatment often is the deciding factor which makes for success. A patient should not be considered ambulatory just because he is able to walk. There is no question about the desirability of treating carriers or patients with mild symptoms as ambulatory, but if a patient has a disease which has caused him more or less discomfort or invalidism for many years, even though these symptoms are mild and occur periodically, he should be put to bed to be given his treatment.

With reference to the value of the case treated by the authors for the purpose of evaluating various remedies, I would seriously question the wisdom of estimating the effect of one drug when closely following another or, as in this case, many others. One remedy may destroy nearly all the amebae and leave those remaining in an attenuated condition so that the result of a succeeding treatment might be misinterpreted. I had such a case recently where at postmortem the amebae were found to exist only in an area about an inch and a half in diameter. Previously distant amebic ulcerations had been demonstrated through the sigmoidoscope.

The past history of the case described by the authors is not an unusual one. It shows intractability to treatment, but by no means justifies the conclusion that none of the drugs used were efficient. An understanding of the pathology of amebiasis shows clearly that we cannot expect to cure some cases unless several courses of treatment are used. In order to compare the value of various remedies the only satisfactory method is to treat a series of cases with each remedy in question, carefully checking the results. No doubt Doctors Anderson and Reed will do this, and I for one hope the drug they are using will prove to be of value.

❋

Doctor Anderson and Doctor Reed (Closing).—Doctor Kessel speaks from an unusually rich experience and many years of accurate observation. We feel, however, that his differentiation between amebic dysentery and "chronic amebiasis" is based on a wrong conception of the natural history of this disease. From the standpoint of the pathology, epidemiology and therapeutics of amebiasis, we feel strongly that James' dictum is correct, that the patient with amebic infection is a constant danger to himself and to others, and should always be treated. We feel that no symptom complex, dysenteric or otherwise, modifies the effectiveness of treatment and, therefore, should not modify the character of treatment. Doctor Kessel rightly refers to the dangers of emetin and its frequent ineffectiveness. Clinically, however, emetin is by no means specific for amebic ulceration. The usefulness of yatren will be discussed below. We have not been concerned about the action of any amebacidal drugs on other protozoa, as we consider their pathogenicity at least doubtful and in any case relatively negligible in comparison with *E. histolytica*. Stovarsol is decidedly unsatisfactory because of its high toxicity. Agreeing with James' opinion, we can consider only protozoölogic cure as the goal to be achieved.

Doctor Gunn's discussion illustrates nicely the very points which have led us to seek new drug agents for the cure of amebiasis. His reference to the dangers of emetin when used "in overdoses or injudiciously" is strong evidence for the need of a new and different drug. Our paper did not make the claim, nor conclude, that "no drugs or treatments have been advocated that are efficacious." Reference to the paper itself will show clearly the points on which all treatments advocated to date are *unsatisfactory*. The method of treatment advocated by Doctor Gunn illustrates this very point. In the first place, it includes an emetin course, with the attached risks that Doctor Gunn has emphasized. It is to be reiterated that even judicious use of emetin within average safe limits does *not* remove but only minimizes toxic effects. Secondly, it requires bed rest. This is expensive for the patient and often economically impossible. It also, like the emetin injections and the general prolonged length of treatment, adds seriously to the patient's cost in time and in money. Any type of treatment that adds seriously to the patient's cost in time, in drug cost and in medical fees, is decidedly unsatisfactory and should lead to search for better methods. Thirdly, the drug cost is high. Chiniofon, which is the official name under which some half-dozen proprietaries are marketed, is the name which should be used instead of yatren. It is essentially the same as anayodin which has less iodin content. The amount Doctor Gunn prescribes costs the patient, at retail, approximately $12. Ten grains of emetin in hypo tablets average $3 to the patient. Three doses of neoarsphenamin (0.9 gram) cost approximately $6. Thus the drug cost to the patient approximates $21. In addition the patient must pay for physician's visits and must lose much time, with only an 80 to 90 per cent chance of cure. Evidently a more effective treatment, costing the patient less than $2 complete for drugs, would be more satisfactory.

Our own experience with the older methods of treatment parallels that of Doctor Gunn in percentage of protozoölogic cures. In view of the high toxicity and expense of these methods, we can hardly agree that they have reached a degree of specificity approaching that in malaria. But even if such were the case they would still be unsatisfactory for the exact reasons enumerated and because the treatment of malaria itself has by no means reached a satisfactory state of specificity. Doctor Gunn's statement that a patient with a disease which has caused him more or less discomfort or invalidism for many years should be put to bed to be given his treatment can scarcely be accepted as a general rule in medical practice.

In the present paper it has been our aim to illustrate from a practical case the disadvantages of the older treatment of amebiasis. The discussions above confirm our belief that improved methods are needed. The advantage of an oral ambulatory method of low cost, low toxicity, and high efficiency would seem self-evident.

CHRONIC THYROIDITIS*

By Whitfield Crane, M. D.
Oakland

Discussion *by D. Schuyler Pulford, M. D., Woodland; Verne Carlton Hunt, M. D., Los Angeles; Clarence G. Toland, M. D., Los Angeles.*

THE problems arising in the diagnosis and treatment of thyroid dysfunction are of absorbing interest to the internist, surgeon, and pathologist. There is a great deal that we do not know, but with the fairly universal adoption of practical classifications of goiter the diagnosis and treatment of the well known types have been more or less standardized. There is, however, one peculiar disease entity of the thyroid that until the last few years has received comparatively little attention in this country. This is the

* Read before the General Surgery Section of the California Medical Association at the sixtieth annual session, San Francisco, April 27-30, 1931.